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Distinct roles of microRNA-1 and -499 in ventricular specification and maturation of human embryonic stem cells

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Aims and Methods: MicroRNAs (miRs) negatively regulate transcription and are important determinants of normal heart development and heart failure pathogenesis. Despite the significant knowledge gained in mouse studies, their functional roles in human (h) heart remain elusive. We hypothesised that miRs that figure prominently in cardiogenesis are differentially expressed in differentiating, developing, and terminally mature human cardiomyocytes (CMs).

Results: As a first step, we mapped the miR profiles of human (h) embryonic stem cells (ESCs), hESC-derived (hE), fetal (hF) and adult (hA) ventricular (V) CMs. 63 miRs were differentially expressed between hESCs and hE-VCMs. Of these, 29, including the miR-302 and -371/372/373 clusters, were associated with pluripotency and uniquely expressed in hESCs. Of the remaining miRs differentially expressed in hE-VCMs, 23 continued to express highly in hF- and hA-VCMs, with miR-1, -133, and -499 displaying the largest fold differences; others such as miR-let-7a, -let-7b, -26b, -125a and -143 were also significantly expressed in h fibroblasts, indicating non-cardiac specificity. Functionally, LV-miR-499 transduction of hESC-derived cardiovascular progenitors significantly increased the yield of hE-VCMs (to 72% from 48% of control; $P<0.05$) and contractile protein expression without affecting their electrophysiological properties ($P>0.05$). By contrast, LV-miR-1 transduction did not bias the yield ($P>0.05$) but decreased ADP and hyperpolarised RMP/MDP in hE-VCMs due to increased I_{to}, I_{Ks} and I_{Kr}, and decreased I_f ($P<0.05$) as signs of maturation. Also, LV-miR-1 but not -499 augmented the immature Ca^{2+} transient amplitude and kinetics.

Conclusion: Based on these and additional molecular pathway analyses, we conclude that miR-1 and -499 play differential roles in human cardiogenesis, and their effects are context dependent. While miR-499 promotes ventricular specification of hESCs, miR-1 serves to facilitate electrophysiological maturation.

An event-related potential study on the information flow during prospective memory interference

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Background: Electroencephalography (EEG) can examine the temporal sequence of brain activity related to a specific event, which is referred to as event-related potential (ERP). Prospective memory (PM) interference presents the interference effect of an embedded PM task on other ongoing task. In the previous functional MRI study, we found that the fusiform gyrus, left inferior parietal lobe and left frontal lobe play an essential role in PM interference effect. However, little temporal information could be retrieved from the functional MRI data.

Methods: Six young subjects participated in the present ERP study on PM task. The PM task was the same as that in fMRI. Briefly, there were ongoing and PM condition, both of them had four blocks of 42s task and 18s rest. The ERP data were collected by NeuroSCAN machine. Preliminary average data of each participant were preprocessed by SCAN software, then they were further processed by the EEG function in SPM software.

Results: Behavioural data showed that the reaction time of pure ongoing trial, contaminated ongoing trial and PM trial were 354, 391, 467 ms, and their accuracy were 99%, 99% and 95%, respectively. ERP data showed that no significant difference of EEG between pure and contaminated ongoing was found in the occipital lobe at about 150 ms after stimuli presentation, then it spread to the temporo-occipital lobe at around 332-350 ms, to the prefrontal area at 566 ms, then to the posterior parietal lobe at 619 ms, finally to the posterior frontal lobe at 725-746 ms.

Conclusion: The ERP data are largely concurred with fMRI result with regard to location. Additionally, it showed that brain activity related to PM interference may initiate at the temporo-occipital lobe, then spread to the prefrontal area, posterior parietal lobe, finally to the posterior frontal lobe. Such ERP data demonstrated the information flow of PM interference in young adults.

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